CLAIMS

We claim:

1. An isolated polypeptide consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO.: 1, SEQ ID NO.: 2, SEQ ID NO.: 3, SEQ ID NO.: 4, SEQ ID NO.: 5, SEQ ID NO.: 6, and SEQ ID NO.: 7.

2. An isolated polypeptide consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO.: 8, SEQ ID NO.: 9, SEQ ID NO.: 10, SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, and SEQ ID NO.: 15.

3. A pharmaceutical preparation for tolerization comprising a pharmaceutically acceptable carrier and

an amount of an isolated human polypeptide effective for tolerizing an individual to an autoantigen, said human polypeptide including an amino acid sequence corresponding to a sequence motif for an HLA-DR protein;

wherein said HLA-DR protein is associated with a human autoimmune disease;

wherein said polypeptide binds to said HLA-DR protein;

wherein said polypeptide bound to said HLA-DR protein activates autoreactive T cells from a subject having said autoimmune disease; and

wherein said polypeptide is a non-collagen and non-myelin basic protein polypeptide.

4. The pharmaceutical preparation of claim 3 wherein said HLA-DR protein is an HLA-DR4 protein and said autoimmune disease is pemphigus vulgaris.

5. The pharmaceutical preparation of claim 4 wherein said motif is PV motif #1.

6. The pharmaceutical preparation of claim 4 wherein said amino acid sequence consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO.: 1, SEQ ID NO.: 2, SEQ ID NO.: 3, SEQ ID NO.: 4, SEQ ID NO.: 5, SEQ ID NO.: 6, and SEQ ID NO.: 7.

7. A pharmaceutical preparation for tolerization comprising a pharmaceutically acceptable carrier and

an amount of an isolated human pathogen polypeptide effective for tolerizing an individual to said polypeptide, said polypeptide including an amino acid sequence corresponding to a sequence motif for an HLA-DR protein;

wherein said HLA-DR protein is associated with a human autoimmune disease;

wherein said polypeptide binds to said HLA-DR protein; and

wherein said polypeptide bound to said HLA-DR protein activates autoreactive T cells from a subject having said autoimmune disease.

8. The pharmaceutical preparation of claim 7 wherein said HLA-DR protein is an HLA-DR2 protein and said autoimmune disease is multiple sclerosis.

9. The pharmaceutical preparation of claim 8 wherein said motif is selected from the group consisting of MS motif #1, MS motif #2 and MS motif #3.

10. The pharmaceutical preparation of claim 8 wherein said amino acid sequence consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO.: 8, SEQ ID NO.: 9, SEQ ID NO.: 10, SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, and SEQ ID NO.: 15.

11. A method of tolerizing an individual to an autoantigen of pemphigus vulgaris comprising

administering an effective amount of the pharamaceutical preparation of any one of claims 4-6 to a subject in need of such treatment.

12. A method of tolerizing an individual to a foreign antigen implicated in multiple sclerosis comprising

administering an effective amount of the pharmaceutical preparation of any one of claims 8-10 to an individual in need of such treatment.

13. A pharmaceutical preparation for vaccinating an individual at risk of an autoimmune disease comprising a pharmaceutically acceptable carrier and

an amount of an immunogenic preparation effective to immunize against a human pathogen that in its native form includes a polypeptide having an amino acid sequence corresponding to a sequence motif for an HLA-DR protein;

wherein said HLA-DR protein is associated with said autoimmune disease;

wherein said polypeptide binds to said HLA-DR protein;

wherein said polypeptide bound to said HLA-DR protein activates autoreactive T cells from a subject having said autoimmune disease; and

wherein said preparation is free of a polypeptide corresponding to said sequence.

14. The pharmaceutical preparation of claim 13 wherein said HLA-DR protein is an HLA-DR4 protein and said autoimmune disease is pemphigus vulgaris.

15. The pharmaceutical preparation of claim 14 wherein said motif is PV motif #1.

16. The pharmaceutical preparation of claim 14 wherein said amino acid sequence consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO.: 1, SEQ ID NO.: 2, SEQ ID NO.: 3, SEQ ID NO.: 4, SEQ ID NO.: 5, SEQ ID NO.: 6, and SEQ ID NO.: 7.

17. The pharmaceutical preparation of claim 13 wherein said HLA-DR protein is an HLA-DR2 protein and said autoimmune disease is multiple sclerosis.

18. The pharmaceutical preparation of claim 17 wherein said motif is selected from the group consisting of MS motif #1, MS motif #2 and MS motif #3.

19. The pharmaceutical preparation of claim 17 wherein said amino acid sequence consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO.: 8, SEQ ID NO.: 9, SEQ ID NO.: 10, SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, and SEQ ID NO.: 15.

20. A method of vaccinating an individual at risk of pemphigus vulgaris comprising

administering an effective amount of the pharmaceutical preparation of any one of claims 14-16.

21. A method of vaccinating an individual at risk of multiple sclerosis comprising

administering an effective amount of the pharmaceutical preparation of any one of claims 17-19.

22. The pharmaceutical preparation of claim 17 wherein said pathogen and said peptide are selected from the group consisting of the respective pairs Herpes simplex virus and UL15 protein, Herpes simplex virus and SEQ ID NO.: 8, Adenovirus and Adenovirus ORF protein, Adenovirus and SEQ ID NO.: 09, Pseudomonas aeruginosa and phosphomannomutase protein, Pseudomonas aeruginosa and SEQ ID NO.: 10, Papillomavirus and L2 protein, Papillomavirus and SEQ ID NO.: 11, Epstein-Barr virus and DNA polymerase protein, Epstein-Barr virus and SEQ ID NO.: 12, Influenza virus and hemagglutinin protein, Influenza virus and SEQ ID NO.: 13, Reovirus and sigma 2 protein, Reovirus sand SEQ ID NO.: 14, Herpes simplex virus and DNA polymerase, and Herpes simplex and SEQ ID NO.: 15.

23. A method of evaluating a peptide for an ability to induce an autoimmune response comprising the steps of

(1) choosing an MHC HLA-DR molecule associated with said autoimmune response, said MHC molecule having major MHC binding pockets designated P1, P4, P6, P7 and P9, each said pocket binding an amino acid residue at a corresponding relative position, Px, of an epitope;

(2) selecting a first major MHC binding pocket Pi and a second major MHC binding pocket Pj;

(3) identifying a first set of amino acid residues which bind within said first pocket, identifying a second set of amino acid residues which bind within said second pocket; and

(4) comparing an amino acid sequence of said peptide to a sequence motif wherein said motif includes said first set of amino acid residues at a relative position Pi and said second set of amino acid residues at a relative position Pj.

24. The method of claim 23

wherein said epitope is an epitope of known amino acid sequence and wherein said epitope has TCR contact residues designated P-1, P2, P3, P5, P8 and P11;

wherein step (2) further comprises selecting a first TCR contact point at a relative position Pk of said epitope and wherein step (3) further comprises identifying a third set of amino acid residues which bind a TCR at said contact point, and

wherein said motif includes said third set of amino acid residues at a relative position Pk.

25. The method of any one of claims 23 and 24 wherein said first binding pocket is a P1 pocket and said second binding pocket is selected from the group consisting of a P4 pocket and a P6 pocket.

26. A method of identifying foreign antigens implicated in human autoimmune response comprising the steps of

(1) choosing an MHC HLA-DR molecule associated with said autoimmune response, said MHC molecule having major MHC binding pockets designated P1, P4, P6, P7 and P9, each said pocket binding an amino acid residue at a relative position Px of an epitope;

(2) selecting a first major MHC binding pocket Pi and a second major MHC binding pocket Pj;

(3) identifying a first set of amino acid residues which bind within said first pocket, identifying a second set of amino acid residues which bind within said second pocket;

(4) defining a sequence motif wherein said motif includes said first set of amino acid residues at a relative position Pi and said second set of amino acid residues at a relative position Pj;

(5) identifying a set of human pathogen peptide sequences corresponding to said motif.

27. The method of claim 26 further comprising the step of excluding from said set sequences from at least one species in a normal human intestinal flora.

28. The method of claim 26 further comprising the step of excluding from said set sequences from at least one species of pathogen negatively correlated with the incidence of said response.

29. The method of claim 26 wherein step (5) includes a search of a computer database using said motif as a search criterion.